

What is Claimed is:

1. A method of preparing an elastomeric gasket material for use in a metered dose inhaler, said method comprising:

5 contacting an elastomeric gasket material to be used in a metered dose inhaler, which gasket material comprises one or more extractable compounds, with a solution comprising an organic solvent, wherein the solution is at a temperature of at least 40°C to extract at least a portion of at least one of the one or more extractable compounds from the elastomeric gasket material.

10 2. The method of claim 1, wherein the elastomeric gasket material comprises acrylonitrile butadiene rubber.

15 3. The method of claim 1, wherein at least one of the one or more extractable compounds is selected from the group consisting of nonylphenol isomers, 2,2'-methylenebis(6-tertbutyl-4-methylphenol), 2,2,4,6,6-pentamethylhept-3-ene, 3'-oxybispropanitrile, oleic acid, palmitic acid, and stearic acid.

20 4. The method of claim 1, wherein at least one of the one or more extractable compounds has a vapor pressure greater than 45 torr (6000 Pa) at a temperature of 20°C.

5. The method of claim 1, wherein the solution comprises a lower alcohol.

25 6. The method of claim 5, wherein the solution further comprises an acid.

7. The method of claim 6, wherein the solution has a pH less than 5.5.

8. The method of claim 6, wherein the solution has a pH between 2.5 and 6.0.

30 9. The method of claim 5, wherein the lower alcohol is ethanol or isopropanol.

10. The method of claim 5, wherein the solution consists essentially of ethanol.

11. The method of claim 1, wherein the elastomeric gasket material is contacted with the solution for at least 1 hour.

12. The method of claim 1, wherein the elastomeric gasket material is contacted with the solution at a temperature of at least 60°C.

13. The method of claim 1, wherein the elastomeric gasket material is contacted with the solution under reflux conditions for the solution.

14. The method of claim 1, wherein the elastomeric gasket material is contacted with the solution in the presence of ultrasonic energy.

15. The method of claim 1, wherein the elastomeric gasket material is contacted with the solution under conditions sufficient to extract at least 20 percent of at least one of the one or more extractable compounds.

16. The method of claim 1, wherein the elastomeric gasket material is contacted with the solution under conditions sufficient to extract at least 40 percent of at least one of the one or more extractable compounds.

17. The method of claim 1, further comprising agitating the elastomeric gasket material.

18. The method of claim 17, wherein the agitating of the elastomeric gasket material is performed subsequent to the contacting of the elastomeric gasket material with the solution.

19. The method of claim 18, further comprising contacting the elastomeric gasket material with the solution subsequent to the agitating of the elastomeric gasket material.

20. A method of making an elastomeric sealing gasket for use in a metered dose inhaler, said method comprising:

contacting an elastomeric gasket material configured to be used in a metered dose inhaler, which gasket material comprises one or more extractable compounds, with a solution comprising an organic solvent under conditions sufficient to extract a portion of

at least one of the one or more extractable compounds from the elastomeric gasket material; and

forming a sealing gasket from the elastomeric gasket material.

5 21. The method of claim 20, wherein the contacting of the elastomeric gasket material occurs after the forming of the sealing gasket.

22. The method of claim 20, wherein the forming of the sealing gasket comprises cutting the sealing gasket material to provide the sealing gasket.

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23. The method of claim 21, wherein the sealing gasket material is in the shape of a sheet of sealing gasket material.

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24. The method of claim 21, wherein the sealing gasket material has a thickness between 0.5 and 2 mm.

25. A method of making an elastomeric MDI sealing gasket comprising:

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contacting a base polymer starting material that comprises one or more extractable compounds with a solution comprising an organic solvent under conditions sufficient to extract at least a portion of at least one of the one or more extractable compounds from the base polymer starting material to provide a treated raw polymer material;

producing elastomer from the treated raw polymer material; and

forming an MDI gasket from the elastomer.

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26. A method of making an elastomeric MDI sealing gasket comprising forming an MDI gasket from a piece of elastomer that has been produced from base polymer starting material that comprises one or more extractable compounds and has been contacted with a solution comprising an organic solvent under conditions sufficient to extract at least a portion of at least one of the one or more extractable compounds from the base polymer starting material.

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27. A sealing gasket for use in an MDI which sealing gasket has been treated by a method as claimed in any one of claims 1 to 19 or has been made according to a method as claimed in any one of claims 20 to 26.

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28. A sealing gasket for use in an MDI comprising:

an elastomeric gasket material; and
between 0.04 and 0.17% oleic acid.

5 29. A sealing gasket as claimed in claim 28, further comprising between 0.05 and 0.35
palmitic acid.

30. A sealing gasket as claimed in claim 28 or 29, further comprising between 0.03 and
0.12 elaidic acid.

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31. A sealing gasket as claimed in any of claims 28 through 30, further comprising
between 0.06 and 0.12 stearic acid.

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32. A method of manufacturing an MDI comprising providing an MDI sealing gasket as
claimed in claim 27, providing the other MDI components and a pharmaceutical aerosol
formulation and assembling the MDI.

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33. A method as claimed in claim 32 wherein the pharmaceutical aerosol formulation
comprises salmeterol xinafoate, fluticasone propionate or a combination of those with
each other or with one or more further medicaments.

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34. A metering valve suitable for metering a drug suspension comprising a medicament
and a propellant, which metering valve comprises a valve body, a metering chamber, a
valve stem and one or more sealing gaskets as claimed in any one of claims 27 through
31.

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35. A container comprising a canister sealed with a metering valve and a sealing gasket,
which canister contains a pharmaceutical aerosol formulation comprising a propellant
and a medicament, wherein the sealing gasket is one as claimed in any one of claims 27
through 31.

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36. A container as claimed in claim 35, wherein the pharmaceutical aerosol formulation
comprises between a lower limit of 0.7 and an upper limit of 7.0 µg of palmitic acid after
storage at 40°C for 2 weeks.

37. A container as claimed in claim 35 or 36, wherein the pharmaceutical aerosol formulation comprises between a lower limit of 0.7 and an upper limit of 7.0 μg of oleic acid after storage at 40°C for 2 weeks.

5 38. A container as claimed in any one of claims 35 through 37, wherein the pharmaceutical aerosol formulation comprises between a lower limit of 0.0 and an upper limit of 0.4 μg of elaidic acid after storage at 40°C for 2 weeks.

10 39. A container as claimed in any one of claims 35 through 38, wherein the pharmaceutical aerosol formulation comprises between a lower limit of 0.0 and an upper limit of 4.0 μg of stearic acid after storage at 40°C for 2 weeks.

15 40. A metered dose inhaler comprising a canister in communication with a metering valve suitable for metering a drug suspension comprising a medicament and a liquid propellant, wherein the metering valve and the canister are sealed with a sealing gasket as claimed in any one of claims 27 through 31.

20 41. A drug product comprising a canister containing a drug suspension comprising a propellant and a medicament in communication with a metering valve suitable for metering a drug suspension comprising a medicament and a liquid propellant, wherein the metering valve and the canister are sealed with one or more sealing gaskets as claimed in any one of claims 27 through 31.

25 42. A package comprising a metered dose inhaler as claimed in claim 32 contained within a flexible wrapper, said wrapper being composed of a material that is substantially permeable to evacuation of propellant gas and substantially impermeable to intrusion of atmospheric moisture.

30 43. A method of treating asthma or COPD in a patient which comprises use by the patient of a metered dose inhaler as claimed in claim 32.

35 44. A method of prolonging the shelf-life of a metered dose inhaler drug product comprising assembling the metered dose inhaler from parts including one or more sealing gaskets as claimed in any one of claims 27 through 31.

45. Use of a sealing gasket as claimed in any one of claims 27 through 31 in a method of manufacturing an MDI for providing a dispensed drug aerosol with higher FPM than an MDI with an untreated sealing gasket.

5 46. Use of a sealing gasket as claimed in any one of claims 27 through 31 in a method of manufacturing an MDI for providing a dispensed drug aerosol with higher FPM storage stability than an MDI with an untreated sealing gasket.

10 47. Use of pure ethanol in a seal or gasket extraction for providing a seal or a gasket which, when incorporated into an MDI provides an MDI which has a dispensed drug aerosol with higher FPM than an MDI with an untreated sealing gasket.

15 48. Use of pure ethanol in a seal or gasket extraction for providing a seal or a gasket which, when incorporated into an MDI provides an MDI which has a dispensed drug aerosol with higher FPM storage stability than an MDI with an untreated sealing gasket.